International Journal of Surgery Open 10 (2018) 66–71

Contents lists available at ScienceDirect

International Journal of Surgery Open

journal homepage: www.elsevier.com/locate/ijso

Research Paper

Performance characteristics of multiparametric-MRI at a non-academic hospital using transperineal template mapping biopsy as a reference standard

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ARTICLE INFO

Article history:
Received 4 January 2018
Accepted 7 January 2018
Available online 31 January 2018

Keywords:
Magnetic resonance imaging
Needle biopsy
Prostatic neoplasm
Predictive value of tests

ABSTRACT

Objectives: To evaluate diagnostic accuracy of mpMRI in a non-academic hospital using transperineal template prostate mapping (TPM) biopsy as a reference standard. Secondary objectives included evaluating why mpMRI missed significant cancer.

Materials and methods: 101 men received pre-biopsy mpMRI and TPM-biopsy over 16 months. Disease status was assigned at hemigland level. Primary histological definition of clinical significance was Gleason grade >/ = 4 + 3 or maximum cancer core length (MCCL) >/ = 6 mm. Positive mpMRI was defined as Prostate Imaging Reporting and Data System (PI-RADS) score >/ = 3.

Results: Median age 69 (IQR 62–76). Median PSA 7 ng/ml (IQR 4.6–9.8). mpMRI had sensitivity 76.9%, specificity 60.7%, PPV 40.4% and NPV 88.3% at primary definitions. For detecting any Gleason >/ = 7 mpMRI had sensitivity 73.2%, specificity 60.3%, PPV 41.4% and NPV 85.4%. Mean MCCL was lower where significant cancer was missed compared to those correctly identified (5.8 mm versus 7.7 mm respectively, p = 0.035).

Conclusion: mpMRI performance characteristics were very encouraging when compared to contemporary clinical trials. In a non-academic hospital setting, negative mpMRI was just as good at ruling-out significant disease, though the ability of positive mpMRI to accurately detect significant disease was lower. An mpMRI-guided diagnostic pathway should be accompanied by appropriate mpMRI protocol optimisation, training, and quality control.

1. Introduction

Transrectal ultrasound (TRUS) guided prostate biopsy is the standard of care for prostate cancer diagnosis in many countries [1]. It is routinely carried out under local anaesthetic and is relatively easily learnt, taught and applied, making it a practical diagnostic strategy. However, it has several recognised limitations and is prone to random and systematic error [2]. Anterior lesions are frequently missed, reducing accuracy [3]. Additionally, they can lead to urosepsis in 1–6% [4].

The use of magnetic resonance imaging (MRI) in the prostate cancer pathway has seen growing interest due to advances in technology using a multiparametric approach (mpMRI). This involves T1 and T2 weighted images (T2W) combined with functional imaging sequences such as diffusion weighted imaging (DWI) and dynamic contrast enhancement (DCE) [5,6]. If biopsy could be avoided in men with negative mpMRI then routine use of pre-biopsy mpMRI could be a cost-effective strategy compared to TRUS-biopsy [7]. However, as a relatively novel modality, routine integration of pre-biopsy mpMRI into national diagnostic cancer pathways has yet to occur.

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https://doi.org/10.1016/j.ijso.2018.01.002

Data from experienced academic centres and contemporary clinical trials show the negative predictive value (NPV) for detection of significant cancer for mpMRI ranges from 72 to 92% [8–11] and targeted-only approaches have been shown to detect similar amounts of significant cancer to systematic biopsy [12,13]. Randomised studies have shown that MRI performance may be influenced by whether the centre was a dedicated high volume mpMRI academic centre or a non-academic centre, with better performance of an MRI-guided pathway demonstrated in the academic centre [14] than outside of one [15]. It is thus known that optimisation of MRI scanners and the centre's experience has an important role in mpMRI performance as a diagnostic tool [16]. However, mpMRI has not been validated in non-tertiary referral ("non-academic") centres against a thorough reference standard of transperineal template mapping biopsy (TPM).

The primary objective of this study was to evaluate the diagnostic accuracy of mpMRI in a non-tertiary referral centre using TPM biopsy as a reference standard. Secondary objectives were to assess: the additional value of DCE and high b-values on DWI in detecting cancer and to explore reasons why mpMRI missed significant cancer.

2. Material and methods

2.1. Setting

Princess Alexandra Hospital (PAH), a non-academic hospital, receiving the majority of its referrals for men with suspected prostate cancer directly from family doctors.

2.2. Patient cohort

All consecutive men who had a TPM biopsy between January 1st, 2015 and April 30th, 2016 were identified from the histopathology database. The population consisted of a representative cohort of all men indicated for prostate biopsy including: 1) biopsy naïve men with suspicion of prostate cancer, 2) men with previous negative biopsy but continued suspicion of prostate cancer and 3) men with known low risk prostate cancer confirmed on a previous biopsy on active surveillance. All men underwent prostate mpMRI and went on to biopsy regardless of mpMRI findings. Men were excluded if the mpMRI was carried out at a different institution or if it was known in advanced that major MRI artefact would be present (e.g. pelvic metalwork).

2.3. Transperineal biopsy

TPM biopsy was performed under general anaesthesia using a modified Barzell technique, reported previously [17]. Biopsy cores were taken approximately every 5 mm on the transperineal grid, aiming for a sampling density of 1 biopsy per ml of tissue. Biopsy cores were potted separately into one of 12 pots. Where mpMRI identified a suspicious lesion, additional targeted biopsies were taken using visual registration technique [12]. One of three experienced surgeons with three to six years of experience in transperineal prostate biopsy carried out the procedures.

2.4. Magnetic resonance imaging

mpMRI was performed with one of two scanners (1.5T Siemens Avanto and 1.5T Siemens Essenza). Sequences included T2W and DWI imaging for all patients, DCE was introduced after January 2015. Contrast used was 15 ml Dotarem® (gadoterate meglumine) administered at 3 mls/sec (concentration 279.32 mg/ml). All cases used a pelvic phased array coil without endorectal coils.

mpMRIs were reported by one of three consultant radiologists with experience in prostate mpMRI ranging from five to twelve years. Prostate lesions were scored using five-level PI-RADS scale (1—cancer highly unlikely, 2—cancer unlikely, 3—equivocal, 4—cancer likely, 5—cancer highly likely) and scores allocated into 27 sectors. Scoring prior to October 2015 was performed using PI-RADSv1 [18]. After this, PI-RADSv2 guidelines were adopted [5]. Dedicated high b-values (>/ = 1000) were introduced from August 2015. Detailed sequence parameters are shown in Supplementary Table 1.

2.5. Prostate specimens

Specimens were analysed according to guidelines set by the Royal College of Pathologists, UK [19].

2.6. Clinical significance

Our primary objective was based on using the validated UCL definition 1 (maximum cancer core length [MCCL] >/ = 6 mm of any grade or any amount of Gleason grade >/ = 4 + 3) and PI-RADS score >/ = 3 on mpMRI [10,20]. As there is no accepted universal definition of clinically significant cancer results were reported secondarily according to UCL definition 2 (MCCL >/ = 4 mm or Gleason grade >/ = 3 + 4) and any amount of Gleason grade >/ = 7.

2.7. Re-review of mpMRI

False negative (FN) mpMRIs were re-reviewed by a senior consultant radiologist with pathology results to explore reasons why the initial report was deemed PI-RADS 1–2. Differences in characteristics (PSA level, PSA density, gland volume, total cancer core length (TCCL), and MCCL) between patients with FN and true positive (TP) mpMRIs were compared to identify features that might predict missing cancer.

2.8. Analysis

Prostates were analysed on hemigland level as consistent with previous studies in this field [10].

Statistical analysis was conducted using Microsoft Excel and SPSS version 22 (release 22.0.0.0). 2 × 2 tables to compare presence or absence of clinically significant cancer were created. Sensitivity, specificity, positive predictive value (PPV), NPV, and difference between proportions with 95% CI were calculated where appropriate. Independent T-tests were performed between TP and FN mpMRI results.

2.9. Ethics

This project was deemed exempt from ethics committee approval by the research and development department at PAH.

3. Results

3.1. Study population details

122 men were identified who underwent TPM within the study period. 21 were excluded (1 had mpMRI from another site, 5 had major artefacts from metalwork, and 15 did not have a pre-biopsy mpMRI). Median age was 69, median PSA was 7.0 ng/ml and median prostate volume was 42 ml 24/101 (24%) had no mpMRI lesion; 76/101 (75%) had a PI-RADS score of >/ = 3 (Table 1).

Overall detection of all cancer on TPM biopsy was 78/101 (77%). 41/101 (41%) had cancer diagnosed with UCL definition 1; 57/101